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April 1, 2013

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TSCA Confidential Business Information Center (7407M)

EPA East – Room 6428

Attn: Section 8(e)

U.S. Environmental Protection Agency

12000 Pennsylvania Avenue, NW

Washington DC 20460-0001



CONTAINS CONFIDENTIAL BUSINESS INFORMATION

To Whom It May Concern: .

[CBI] is providing notice to the U.S. Environmental Protection Agency (“EPA”) regarding [CBI], under Section 8(e) of the Toxic Substances Control Act (“TSCA”) concerning information that [CBI] received from a contract laboratory conducting a test on the substance. This substance is subject to the TSCA Section 5(e) Consent Order issued for [CBI].

The initial information from the laboratory suggests that the adverse effects observed are the result of certain test conditions, as described below, and thus do not reasonably support a conclusion that the chemical substance being tested presents a substantial risk of injury to health or the environment. Nonetheless, [CBI] has decided to err on the side of caution and submit a Section 8(e) notification.

The laboratory is conducting a Pharmacokinetic (“PK”) test. In the Tier One study, some mice are dosed with a single low dose administration (30 mg/kg body weight) and some with a single high dose administration (300 mg/kg body weight).



Company Sanitized

On March 5, 2013, [CBI] received information that 3 high dose male mice (300 mg/kg, single dosing) housed in “metabowl” cages, sealed environments meant to allow testing of all expired air, urine and feces, were found dead, and that a low dose male mouse (30 mg/kg, single dosing), also in a metabowl cage, was suffering and was humanely killed. Furthermore, some male high dose mice in regular cages were also found, subsequently, to have milder clinical effects from which they fully recovered. There were no fatalities or required euthanasia in the mice in the regular cages.

The protocol for this test was accepted by EPA under the 5(e) order. The 300 mg/kg, single dose high dose administration was previously determined as appropriate under a dose range-finding test. There were no fatalities or severe clinical effects in that test.

The laboratory has suggested the following:

- Fatalities in the metabowl cages are attributed to extra stress in that environment. They have stated that mice in that environment are often unable to compensate adequately for loss of body heat, and it is difficult to recover from even relatively minor clinical effects.
- Clinical signs in the non-metabowl high dose mice were consistent with what would be expected in a high dose group for this kind of a PK study.
- The death of the low dose male mice can be attributed solely to the added stress of the metabowl cage.

We have also attached a sanitized version of this letter. Thank you for your attention to this matter.

Respectfully submitted,

[Signatory; also CBI]